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PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

To:

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NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing
(day/month/year) 08.10.2004

Applicant's or agent's file reference
RCS/PF4877

ATTY FES/EAR/MI
N/A OR UPDATED ON:
ATTY CHEPPE/MI FES

IMPORTANT NOTIFICATION

International application No.
PCT/EP 03/07612

International filing date (day/month/year)
11.07.2003

Priority date (day/month/year)
12.07.2002

Applicant
GLAXO GROUP LIMITED et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international
preliminary examining authority:



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Form PCT/PEA/416 (January 2004)



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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference RCS/PF4877		FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA416)	
International application No. PCT/EP 03/07612	International filing date (day/month/year) 11.07.2003	Priority date (day/month/year) 12.07.2002	
International Patent Classification (IPC) or both national classification and IPC A61K31/445			
Applicant GLAXO GROUP LIMITED et al.			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of 8 sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the opinion</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>			
Date of submission of the demand 27.01.2004		Date of completion of this report 08.10.2004	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized Officer Johnson, C Telephone No. +49 89 2399-8287 	

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**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/EP 03/07612**

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17):*

Description, Pages

1-74 as originally filed

Claims, Numbers

1-18 received on 07.09.2004 with letter of 03.09.2004

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

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III. Non-establishment of opinion with regard to novelty, Inventive step and Industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1 (part)

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1 (part) are so unclear that no meaningful opinion could be formed (*specify*):

see separate sheet

☒ the claims, or said claims Nos. 1 (part) are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1 (part)

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, Inventive step or Industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-18
	No: Claims	
Inventive step (IS)	Yes: Claims	1-18
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-18
	No: Claims	

2. Citations and explanations

see separate sheet

III. Non-establishment of opinion

In view of a lack of clarity and disclosure (Articles 5 and 6 PCT), claim 1 has only been searched insofar as the prodrugs are acetate, formate or benzoate derivatives of hydroxy, sulfhydryl or amine groups or ester derivatives of carboxylic acid groups. The following examination is performed for completely searched subject matter only.

V. Reasoned statement

Reference is made to the following documents:

D1: Bioorganic & Medicinal Chemistry Letters, 2000, 10(16), 1803-1806

D2: US-A-6048900

Novelty

Compound 3 of D1 differs from the present claims because the linker group corresponding to present group E is n-pentylene.

The general formula in claim 1 of D2 overlaps with present formula (I). However, the present claims may be considered a novel selection, in which R⁵ is Ar¹-piperidyl-n-butylene and R¹ or R² is Ar₂-Ar₃, as such a sub-group is not disclosed in D2.

Claims 1-18 fulfil the requirements of Article 33(2) PCT.

Inventive step

The technical problem underlying the present application appears to be the provision of compounds useful in the treatment of hyperlipidemia. The compound of D1 is a weak chemokine receptor ligand. Those of D2 are useful in the treatment of obesity related disorders such as hyperlipidemia. D2 may therefore be taken as the closest prior art. Although the present compounds are formally encompassed by the general formula of D2, it would be clear to the skilled person that it is not credible that all compounds falling within the general formula (I) of D2 can have qualitatively equivalent activity - the general formula (I) is so broad it encompasses not only the polycyclic compounds illustrated by the examples, but also simple acyclic compounds such as acetamide. The more specific teaching of D2, wherein the R¹-R⁵ substituents have the preferred definitions given in col. 3, l. 20 to col. 4, l. 19 does not encompass the present compounds because of the meaning of the Ar₁ group. Therefore it would not be obvious to solve the above-formulated technical problem by providing the compounds according to claim 1. Thus those claimed compounds which have the alleged activity may be

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP 03/07612

considered inventive.

claims 1-18 fulfil the requirements of Article 33(3) PCT.

Industrial applicability

Claims 1-18 fulfil the requirements of Article 33(4) PCT.